Retrospective analysis of outcome data with regards to the use of Phisio(R)-, Bioline(R)- or Softline(R)-coated cardiopulmonary bypass circuits in cardiac surgery

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Retrospective analysis of outcome data with regards to the use of Phisio®-, Bioline®- or Softline®-coated cardiopulmonary bypass circuits in cardiac surgery

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Abstract

Background: Numerous cardiopulmonary bypass circuits with various coatings designed to reduce the inflammatory response and to provide better hemocompatibility are available. The aim of this study was to compare the effect of phosphorylcholine-coated, albumin-heparin-coated and synthetic polymer-coated perfusion tubing systems on patient outcome. *Methods*: We performed a retrospective database review of elective patients between January 1st 2010 and December 31st 2010. Demographics, preoperative, operative, postoperative data and follow-up were collected and statistically analysed. *Results*: We identified 201 patients and formed three groups: Group 1 with phosphorylcholine coating (n=133), Group 2 with albumin-heparin coating (n=32) and Group 3 synthetic polymer coating (n=36). Mean age was 68±11years, additive Euroscore 5.8±2.7. In-hospital outcomes were comparable between the groups without statistically significant differences. The overall 30-day and 1-year late survival were 98.5% and 96.7±1.9%, respectively. *Conclusions:* Our findings suggest that in-hospital and follow-up outcomes are comparable in cardiac surgery patients after using either phosphorylcholine-coated, albumin-heparin-coated or synthetic polymer-coated circuits during cardiopulmonary bypass.

Keywords

perfusion circuit; Phisio-coated; Bioline-coated; phosphorylcholine-coated; heparin-albumin-coated

Introduction

Cardiopulmonary bypass induces a systemic inflammatory response syndrome, which leads to activation of the complement cascade, oxidative stress and coagulation pathways, resulting in endothelial injury and postoperative organ dysfunction following open heart surgery.[1,2] A number of cardiopulmonary bypass circuits with different coatings are available. These systems have been shown to provide better hemocompatibility with less platelet activation and reduced inflammatory response with less white blood cell adhesions. As a result, less postoperative bleeding and a decreased need of red blood cell transfusion[3] has been reported. Conflicting results are reported with regard to postoperative outcomes following the usage of coated perfusion circuits.[3,4] The aim of this study was to compare the effect of Phisio®- (phosphorylcholine), Bioline®- (albumin-heparin) and Softline®- (heparin-free, synthetic polymer) coated circuits on patient outcome after open heart surgery.

Methods

We performed a retrospective database review within a randomly picked time period (between January 1st 2010 and December 31st 2010) and identified a total of 201consecutive patients with elective aortic valve replacement, on-pump coronary artery bypass graft (CABG) surgery or both combined. Patient demographics, operative and postoperative data, including 24h levels of c-reactive protein, white blood cell count, Quick's test, international

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normalized ratio (INR), creatinine and follow-up were collected and statistically analyzed.

We formed three groups, according to the different biocompatible surfaces of the perfusion systems: Group 1 (Phisio®) used a phosphorylcholine-coated tubing system (n=133); Group 2 (Bioline®) used an albumin-heparin coating (n=32); and Group 3 (Softline®) a synthetic polymer coating (n=36).

Perfusion circuits with the following three different coatings were used: a phosphorylcholine coating (P.h.i.s.i.o.®, Sorin Group, Italy), an albumin-heparin coating (Bioline®, Maquet Cardiopulmonary AG., Hirrlingen, Germany) and a synthetic polymer coating (Softline®, Maquet Cardiopulmonary AG). All perfusion tubing systems were completely coated except for the cannulas. The perfusion systems with Phisio® and Bioline® coatings were standard systems with a priming volume of 1600ml. The Softline®-coated system is a minimized circuit with a priming volume of 1200ml. All perfusion systems contained a hard-shell venous reservoir, used a roller pump and had an arterial filter. The Phisio® systems used the AVANT oxygenator (Sorin, Italy) with which most of the patients were treated because of financial reasons. The Bioline®- and Softline® systems used a Quadrox-i-Adult or a Quadroxy-i Small Adult oxygenator, respectively (Maquet Cardiopulmonary AG). The Bioline® systems were used for operations which were expected to last long, because of their more effective heat exchanger, whereas the Sofline® systems were used for patients below a calculated flow of 5 L/m due to its minimized circuit.

Before cardiopulmonary bypass (CPB) initiation, 300 IU/kg of heparin was administered intravenously in all cases. Re-administration of 5000 IU heparin boluses took place if the activated clotting time (ACT) was lower than 480 seconds on pump. Either antegrade crystalloid Bretschneider or Buckberg blood cardioplegia was used, with moderate hypothermia (32-34°C) or normothermia. After completion of CPB, heparin was antagonized with protamine in a ratio of 1:1.

Statistics: IBM SPSS Statistics 20 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous variables are presented as mean ± standard deviation or median with range and compared between groups, using the Kruskal-Wallis test. The Chi-square test and Fisher's exact test were used to compare proportions. Kaplan-Meier curves were used to analyse survival. P-values less than 0.05 were considered to be statistically significant.

Results

Baseline characteristics were comparable between the groups except for weight, height and hematocrit at admission, which was lower in Group 3. Those patients were meant to be treated with the minimized perfusion system and subsequent reduced priming volume. Accordingly, there were more women in that group (<0.005) (see Table 1).

Operative characteristics are shown in Table 2. Time of surgery, CPB and cross-clamp time, type of surgery and lowest temperature were comparable between the groups.

Table 3 shows the blood results on day one after surgery. C-reactive protein, white blood cell count, Quick's test, INR and creatinine were analyzed. Except for a lower creatinine in Group 3, there were no further significant differences.

Overall in-hospital mortality and stroke rate was 1.5% (n=3) for each. They all occurred in Group 1 (Phisio®). Chest tube drainage, re-exploration for bleeding, red blood cell transfusion, infection, new onset dialysis, postoperative myocardial infarction, ventilation time, ICU stay and hospital stay were comparable between the groups without significant differences.

Median follow-up time was 180 days (32-540 days). Three patients died during follow-up, all in Group 1 (Phisio®). The overall 30-day and 1-year late survivals were 98.5% and 96.7±1.9%, respectively, without significant difference between the groups (95.2 ± 2.7% for Group 1 and 100% for Groups 2 and 3).

Discussion

When heparin was first used in medical devices, it was known to have anti-thrombotic effects.[5] Later, it was proven to have biocompatibility properties as well by inhibiting contact and complement activation and adsorbing lipoproteins, simulating the behaviour of cell membranes.[6,7]

Many trials show that heparin-coated circuits reduce postoperative blood loss and the need for red blood cell transfusion,[3] and ventilation time and ICU stay.[8]

One meta-analysis with 3434 patients in 41 original randomized papers shows that heparin-coated circuits decrease blood loss and red blood cell transfusion by 20%, re-sternotomy by 40%, ventilation by 78 minutes, average ICU stay by 9.3 hours and hospital stay by 0.5 days when compared to non-heparin-bonded circuits. There was also a significant difference in favour of the heparin-coated system regarding death, new onset myocardial infarction, stroke, wound infection and atrial fibrillation.[9]

Sohn et al.[10] showed, in a randomized trial with 73 CABG patients, that heparin-coated and phosphorylcholine-coated circuits induce less inflammatory responses and oxidative stress compared to other circuits. Clinical outcome was not investigated.

Thiara et al.[11] described a comparable degree of in vivo biocompatibility and less inflammatory response in Phisio®- and Bioline®-coated circuits by analyzing

Table 1. Baseline characteristics

	Group 1 Phisio® N=133	Group 2 Bioline® N=32	Group 3 Softline® N=36	P
Age (years)	68±11	67±10	68±13	0.6
EuroSCORE	5.7±2.7	5.3±2.3	6.5±2.8	0.2
Male patients	88 (66.1%)	27 (84.3%)	12 (33.3%)	0.005
Weight (kilograms)	82±15	86±13	63±10	0.005
Height (centimetres)	168±9	169±9	160±8	0.005
Congestive heart failure	11 (8.2%)	6 (18.7%)	4 (11.1%)	0.2
CCS III/IV	30 (22.5%)	10 (31.2%)	8 (22.2%)	0.6
NYHA III/IV	42 (31.5%)	8 (25%)	13 (36.1%)	0.6
Previous myocardial infarction	8 (6%)	4 (12.5%)	2 (5.5%)	0.4
Smoking history	65 (48.8%)	22 (68.7%)	21 (58.3%)	0.1
Diabetes mellitus	33 (24.8%)	7 (21.8%)	5 (13.8%)	0.4
- oral therapy	22 (16.5%)	5 (15.6%)	3 (8.3%)	0.5
- insulin	11 (8.2%)	2 (6.2%)	2 (5.5%)	0.9
Hypertension	97 (72.9%)	23 (71.8%)	22 (61.1%)	0.3
Hypercholesterolaemia	85 (63.9%)	21 (65.6%)	16 (44.4%)	0.08
Creatinine>200micromol/L	4 (3%)	0	1 (2.7%)	1
COPD	19 (14.2%)	3 (9.3%)	4 (11.1%)	0.8
Extracardiac-arteriopathy	15 (11.2%)	6 (18.7%)	4 (11.1%)	0.5
Cerebrovascular disease	5 (3.7%)	3 (9.3%)	0	0.1
Atrial fibrillation	11 (8.2%)	2 (6.2%)	1 (1.7%)	0.5
Haematocrit %	40 (27-48)	41 (35-50)	37 (27-45)	0.005

CCS: Canadian Cardiovascular Society Angina Class; NYHA: New York Heart Association; COPD: chronic obstructive pulmonary disease

Table 2. Operative characteristics

	Group 1 Phisio® N=133	Group 2 Bioline® N=32	Group 3 Softline® N=36	P
Aortic valve replacement	65 (48.9%)	15 (46.9%)	20 (55.6%)	0.6
CABG	40 (30%)	10 (31.3%)	8 (22.2%)	0.6
CABG + Aortic valve	28 (21.1%)	7 (21.8%)	8 (22.2%)	1
Post-op IABP	6 (4.5%)	0	1 (2.7%)	0.7
CPB time (min)	107 (31-330)	110 (58-207)	96 (57-238)	0.6
Cross-clamp (min)	64 (0-142)	74 (0-155)	69 (0-156)	0.2
Time of surgery (min)	210 (115-550)	219 (115-462)	220 (117-449)	0.6
Temperature (°C)	34 (30-37)	34 (32-37)	34 (32-37)	0.9

CABG: coronary artery bypass grafting; IABP: intra aortic balloon pump; CPB: cardiopulmonary bypass

various inflammatory markers. These findings might explain our results, which did not show differences in outcome comparing Phisio®- and Bioline®-coated circuits either.

Tayama et al.[12] were able to show, in a randomized trial of 27 CABG patients, that Bioline® circuits reduce the inflammatory responses when compared to non-heparin coated circuits, although this effect did not appear to have any clinical impact. These findings correlate well with ours.

The beneficial effect of heparin-coating might be due to a reduced systemic heparinization, resulting in reduced blood loss and adverse events.[13,14] There is one randomized trial with 90 patients showing better post-operative outcomes with reduced ventilation times and haemorrhage in high-risk groups (Euroscore +6), using hyaluronan-based heparin-bonded circuits.[15]

It is possible that, in an elective series like ours with routine aortic valve and CABG patients with short CPB and cross-clamp times, there is no evidence of significant

Table 3. Laboratory work 24 hours after surgery

	Group 1	Group 2	Group 3	P
	Phisio®	Bioline®	Softline®	
	N=133	N=32	N=36	
C-reactive protein (ng/l)	54 (8-251)	50 (2-109)	62 (13-211)	0.7
WBC (G/l)	11 (4-25)	10 (6-19)	9 (4-20)	0.1
Quick's test (%)	75 (5.2-123)	75 (40-120)	73 (40-125)	0.8
INR	1.2 (1-1.6)	1.2 (1-1.7)	1.2 (1-1.7)	0.9
Creatinine micromol/L	89 (43-222)	85 (64-188)	78 (39-195)	0.01

WBC: white blood count; INR: international normalized ratio

Table 4. In-hospital outcomes

	Group 1	Group 2	Group 3	P
	Phisio®	Bioline®	Softline®	
	N=133	N=32	N=36	
Mortality	3 (2.2%)	0	0	1
Stroke	3 (2.2%)	0	0	1
Ventilation time (hours)	11 (0-1307)	9 (0-550)	11 (0-217)	0.2
Re-thoracotomy	11 (8.3%)	1 (3.1%)	0	0.1
ICU stay (hours)	23 (0-1961)	24 (0-550)	27 (15-405)	0.06
Hospital stay (days)	9.5 (1-89)	9 (3-29)	10.5 (1-36)	0.4
Drainage (l) (during ICU stay)	0.6 (0.03-8)	0.6 (0.1-5.4)	0.6 (0.08-4)	0.4
RBC (unit until end of ICU stay)	2.2 (0-61)	1.5 (0-19)	2.2 (0-9)	0.9
Myocardial infarction	2 (1.5%)	0	1 (2.7%)	0.7
Dialysis	10 (7.5%)	1 (3.1%)	1 (2.7%)	0.5
Multi-system failure	2 (1.5%)	1 (3.1%)	0	0.4
Pneumonia	12 (9%)	1 (3.1%)	1 (2.7%)	0.3
ARDS	1 (0.7%)	1 (3.1%)	0	0.3
Sepsis	7 (5.2%)	1 (3.1%)	1 (2.7%)	1

ICU: intensive care unit; RBC: red blood cell transfusion; ARDS: acute respiratory distress syndrome

difference in clinical outcome after using Phisio®, Bioline® or Softline® circuits. Therefore, further analysis of high-risk groups (i.e. high Euroscore, emergency procedures, etc.) might reveal clinical and economic advantages that ease decision making for the future.

The limitations of our study are as follows. It is not a controlled study, but an outcome analysis. It is retrospective observational and, therefore, open to selection bias, which may have contributed to the lack of significant differences in outcome (the Softline® group differs from the others, which is explainable by their smaller body size that required the use of this circuit in the first place). Furthermore, the study is not blinded and, therefore, open to treatment bias, which may also have affected the outcome (not just the coatings are different, but also the circuits and the priming volumes). Due to the multiple outcomes, there is the risk of type I statistical error. However, it was our intention to analyze multiple outcomes in order to be able to find any profound differences. No sample size estimation was performed because, in the case of post-hoc analysis, it would go far beyond the limits of this paper.

Conclusion

Our findings suggest that in-hospital and follow-up outcomes are comparable in elective isolated aortic valve, CABG or both combined open heart surgery patients after using either phosphorylcholine-, heparin-albumin- or synthetic polymer-coated circuits during cardiopulmonary bypass. Further analysis of the data is required (cost-benefit of the different circuits, especially in high-risk patients) in order to ease decision making in the future.

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Conflict of Interest Statement

The authors declare that there is no conflict of financial or political interest.

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